

oxidase B) could produce damage to the degenerating nigrostriatal neurons involved in Parkinson's disease. With this information, a large multicenter trial was undertaken comparing the use of an inhibitor of monoamine oxidase B (selegiline) or placebo in the early stages of the disease. The end point was the need for levodopa treatment, indicating a progression of illness. Investigators thought that the use of selegiline slowed the progression of the Parkinson's disease. Critics feel that selegiline is simply a mild antiparkinson medication. This issue should be addressed in future studies, but because selegiline may offer a protective effect and delay the need for levodopa therapy, a regimen of this medication should be started in newly diagnosed patients.

Besides its use as a protective agent early in the disease, selegiline is recognized as an adjunct to levodopa therapy in patients with more advanced disease. It can prolong the effect of levodopa in patients experiencing "wearing-off phenomenon," in which the duration of the effect of levodopa is reduced. Its use is not helpful in patients with the rapidly fluctuating "on-off phenomenon" and may worsen dyskinesias. The dose in both prophylactic and symptomatic therapies is 5 mg by mouth in the morning and at noon. Lower doses may be effective in some patients at a considerably reduced cost. Because of a mild amphetamine effect, the medication should not be given after noon. Side effects are minimal when used alone but greater when combined with levodopa and include nausea, postural hypotension, confusion, and dyskinesias. By starting with half a tablet once a day and slowly increasing the dose as the patient tolerates, it may be possible to establish a dose at which the patient obtains benefit (prolonged levodopa effect) with few side effects. Lowering the dose of levodopa may reduce the side effects of the combination, but it usually also lessens efficacy.

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Intravenous γ -Globulin for Chronic Inflammatory Demyelinating Polyneuropathy and Myasthenia Gravis

IMMUNE GLOBULIN PREPARATIONS extracted from human blood until recently had to be given intramuscularly. Now, preparations of human immune globulin are available that can be infused intravenously safely over several hours. These preparations, purified by cold liquid ethanol fractionation of large pools of human plasma, have not transmitted non-A, non-B hepatitis, human immunodeficiency virus infection, or the acquired immunodeficiency syndrome. Anaphylaxis to intravenous immune globulin can develop, however, in persons with immunoglobulin (Ig) A deficiency, who often have IgG antibodies to IgA.

Intravenous immune globulin has been found useful in the treatment of primary immunodeficiency syndromes, neonatal infections, bone marrow transplantation, chronic lymphocytic leukemia, idiopathic thrombocytopenic purpura, and Kawasaki syndrome. The minimal effective dose in most

of these studies is 150 mg per kg of body weight, and many clinicians feel that higher doses up to 1 gram \cdot kg⁻¹ \cdot day⁻¹ confer superior results.

Dramatic responses to the use of intravenous immune globulin of intractable or progressive chronic inflammatory demyelinating neuropathy have occurred within days of starting treatment at a dose of 400 mg \cdot kg⁻¹ \cdot day⁻¹ for three to five days. A slow rate of infusion, between 40 and 100 ml per hour, of a 5% to 6% solution is recommended to minimize adverse reactions of headache, myalgia, fever, chills, lightheadedness, nausea, or edema. Clinical improvement lasts for months in some cases, while other patients begin to relapse four to six weeks after treatment and may require regular prophylactic outpatient infusions at doses of 150 to 300 mg per kg every one or two weeks. The successful use of intravenous immune globulin in children with acute inflammatory demyelinating neuropathy (or Guillain-Barré syndrome) has recently been reported in abstract form.

Preliminary but favorable results have also been reported for intravenous immune globulin treatment of intractable myasthenia gravis at doses of 0.4 to 1.0 grams \cdot kg⁻¹ \cdot day⁻¹ for five days. Clinical improvement can begin within nine days of starting treatment and last as long as three months, although a second course of intravenous immune globulin may be required because of relapse. A disturbing aspect of intravenous immune globulin treatment of myasthenia gravis is the life-threatening exacerbation that occurs in some patients early in the course of treatment.

In the United States, intravenous immune globulin treatment for a 70-kg person costs more than \$1,000 per day, which is perhaps no more expensive than plasma exchange, and it is apparently safer than long-term prednisone or immunosuppressive therapy. The efficacy and safety of intravenous immune globulin, however, compared with plasma exchange and prednisone therapy, for either chronic inflammatory demyelinating neuropathy or myasthenia gravis have not yet been established by controlled clinical trials.

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Botulinum Toxin Therapy

BOTULINUM TOXIN is a potent neurotoxin that binds to the extracellular portion of the nerve terminal membrane and inhibits transmission across the neuromuscular junction. The effect of the toxin is gradual, lasts for several months, and can lead to denervation atrophy of the involved muscle. Doses of botulinum toxin are expressed in mouse median lethal dose (LD₅₀) units. The first therapeutic application of botulinum toxin was in strabismus. Botulinum toxin is most useful for strabismic angles of less than 50 prism diopters, postoperative residual strabismus, paralytic strabismus, and cases where surgical intervention is inappropriate. In a few pa-

tients, retrobulbar hemorrhage, eye perforation, double vision, and spatial disorientation may occur. The toxin is also used for spastic entropion, blepharospasm, and hemifacial spasm. The treatment of hemifacial spasm and blepharospasm requires about 25 units. The therapeutic effect lasts, on average, three to four months.

Botulinum toxin therapy is beneficial in spasmodic torticollis. Though improvement could be delayed for as long as two to six weeks, the effect usually starts on the second day, peaks during the first week, and lasts for three months. The treatment of torticollis requires an average of 200 units of toxin, and electromyographic guidance is necessary when deep muscles are injected. Side effects are mild and infrequent and include swallowing difficulties, a temporary increase in spasm or jerking movements, floppy neck, and dysphonia. In one patient, brachial plexopathy occurred after botulinum toxin was administered, and immunologically mediated reactions were suggested. Antibodies to the toxin may develop, rendering further treatment ineffective.

In patients with adductor spasmodic dysphonia, which is characterized by strenuous speech with a staccato, jerky, squeezed, hoarse, groaning voice, administering a small amount of toxin into the laryngeal muscle has been effective. Initial studies used higher doses, but in clinical practice now, only about 5 units are used. Side effects include swallowing difficulties, choking, or a breathy voice, which may last for one or two weeks. An improved voice quality lasts from three to six months after the treatment.

Although botulinum toxin can also be used in treating oromandibular dyskinesia, its use in lingual dystonia should be approached with caution, as it may interfere with swallowing. Other successful applications of botulinum toxin include the treatment of writer's cramp and detrusor sphincter dyssynergia.

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Preventing Chemotherapy-induced Neuropathy

TREATMENT WITH a number of chemotherapeutic drugs is well recognized to result in acute or chronic neurologic injuries. In the evaluation of patients with these injuries, the clinical neurologic examination and testing can be of major importance to reduce or alter the effects of such agents on the peripheral nervous system. In general, the sensory nerve fibers of the peripheral nerves are more susceptible to injury than are the motor or autonomic peripheral nerve structures.

The feet are most commonly affected, and patients usually have numbness, tingling, dysesthesias, or burning sensations. Dysfunction occurs to the dorsal root ganglia or to the

peripheral nerve structures directly. On clinical examination, there may be altered sensation to light touch, cutaneous hypersensitivity, or the results may be normal. Large-fiber sensory dysfunction can be evaluated by testing vibration, proprioception, and kinesthetic perception as well as detecting reduced motor reflexes.

It is essential to evaluate patients by clinical examination before starting chemotherapy. Many patients, particularly elderly persons, may have silent peripheral polyneuropathies from other causes such as alcoholism, nutritional disorders, metabolic problems, and degenerative causes. Some patients may have a remote effect on their peripheral nerves as a result of a paraneoplastic syndrome.

Electrodiagnostic studies can be helpful to determine the extent or progression of a neuropathy. Sensory amplitudes, waveform analysis, latencies, and conduction velocities are the most sensitive studies early in the illness, whereas motor conduction and electromyograms may only become abnormal as the problems progress. Dermatome cutaneous evoked potentials and automated semiquantitative measures of vibratory and thermal sensations can also be used to evaluate peripheral nerve function.

Several therapeutic agents are known to cause peripheral nerve dysfunction, cisplatin being a classic example. The neuropathy is similar to that caused by vitamin E deficiency, and efforts have been made using agents such as ethiofos, adrenocorticotropin analogues, and vitamin E to reduce its severity. Other agents such as vincristine sulfate can produce an autonomic neuropathy with a main presentation of postural hypotension in addition to the polyneuropathy.

Patient instructions are paramount for the early detection of adverse neuropathies associated with chemotherapy. General treatment measures include discontinuation of the drugs, the recognition of underlying treatable neuropathies, and symptomatic treatment.

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Carotid Endarterectomy

THE BENEFIT OF CAROTID ENDARTERECTOMY in preventing stroke is now being clarified by well-conceived randomized trials, 38 years after the procedure was first performed.

The original study of the efficacy of carotid endarterectomy was published in 1970. This is not considered a definitive trial because of design imperfections and a perioperative mortality and morbidity rate of 11%. The strongest trend in the study was toward a benefit for patients with a vessel diameter reduction of 50% or more. Notable stenosis is variously defined as a diameter reduction of 50% to 70% or greater. The method of quantitation is disputed, but higher degrees of stenosis have been the most widely accepted indication for the procedure, particularly in patients with appropriate symptoms.

In 1985 about 107,000 endarterectomies were done in the United States. At the same time, the procedure was criticized as unsubstantiated and overused. Also in 1985, the negative